

Effect of myocardial shortening velocity on duration of electrical and mechanical systole

S₂T interval as measure of shortening rate

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SUMMARY To determine the effect of myocardial shortening velocity on the duration of electrical and mechanical systole, five healthy men, ages 32 to 41, were studied. Carotid massage and atropine were used to define the effects of changes in heart rate without changes in shortening rate. The effects of amyl nitrite, which produced approximately the same degree of tachycardia as atropine but a significantly higher maximum shortening rate, were compared with those of atropine to assess the effects of faster shortening velocities. The increased heart rate produced by both agents caused a substantial decrease in both the QT and the S₁S₂ intervals, but the QT interval was longer and the S₁S₂ interval shorter with the amyl nitrite. Thus, the S₂T interval was substantially longer after amyl nitrite. The results are in keeping with the finding in isolated cardiac muscle that active shortening increases action potential duration and decreases the duration of mechanical activation. These observations raise the possibility that longer QT intervals and shorter S₁S₂ intervals would also be seen in patients with hypokinetic ventricular segments when the healthy muscle contracts more vigorously to compensate for the weaker segments.

Active shortening of isolated cardiac muscle increases the action potential duration,¹ and decreases the duration of mechanical activity.^{2,3} These observations suggest that the electrocardiographically recorded T waves in man might occur later and second heart sounds (S₂) earlier, when ventricular ejection rate increases. If this is so, the interval between the two might be used as an index of myocardial fibre shortening rate. This hypothesis was tested in five healthy volunteers using carotid massage and atropine to define the changes that occur in the time intervals with variation in heart rate but without large changes in fibre shortening. Amyl nitrite was used to increase the velocity of ventricular ejection, and the results obtained with this agent were compared with those during the tachycardia produced by atropine. Myocardial shortening rate was assessed from simultaneous echocardiograms.

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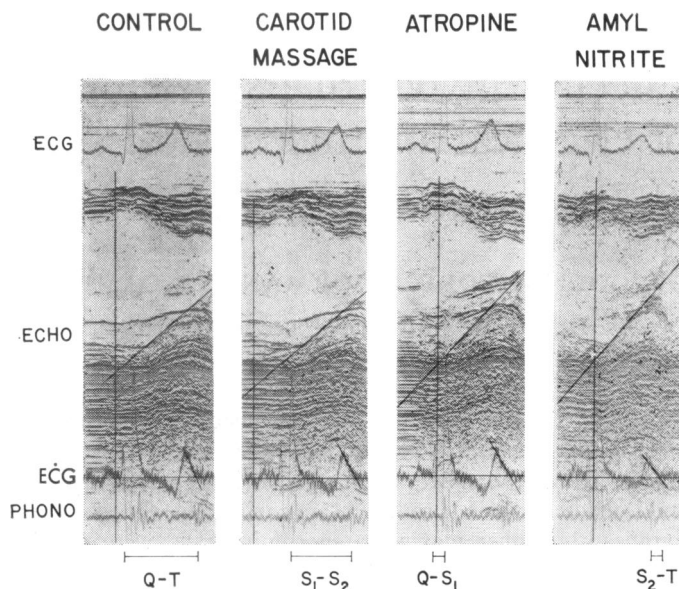
Methods

Five healthy, non-obese men, ages 32 to 41 years, were studied. All were without heart disease and all participated to some degree in regular athletics. They were asked to hold their breath at end expiration during the periods of recording to increase uniformity of conditions and to minimise respiratory interference.

RECORDING

M-mode echocardiograms were obtained with a Unirad 100 Series Echoscope. Left ventricular contraction was measured at a point just below the mitral valve. Simultaneous phonocardiogram, lead II electrocardiogram, and differentiated electrocardiographic traces were displayed on the same recording (Fig. 1). Lead II was used throughout since the T wave vector was closest to this lead in every subject. The use of a single electrocardiograph lead to determine the beginning of the QRS complex and the end of the T wave is justified if the axis of these initial and terminal vectors do not change, as was found in the five subjects studied here. The recorder was run at 78 mm/s (nominal 75 mm/s).

Fig. 1 *Recordings and interventions:* The end of the T wave was determined as the intersection of the two lines drawn through the differentiated electrocardiographic trace (ECG). The phonocardiogram had high and low pass filters set at 100 and 1400 Hz, respectively, throughout all studies. Relative changes in maximum fibre shortening were assessed from the slope of a line drawn through the fastest-moving component of the posterior wall echo. The lines shown here have been darkened for contrast, and obscure some of these echoes.



MEASUREMENTS

Lines were drawn through the zero baseline of the differentiated electrocardiograph trace and through the terminal portion of the T wave on this trace as it approached the baseline (Fig. 1). The end of the T wave was taken as the intersection of these two lines. The timing of the heart sound was taken as the first high frequency component in the phonocardiogram. A vertical line through the timing marks on the record (Fig. 1) served both as a time reference for intervals on different traces and as a vertical reference for measuring the slope of posterior wall motion in the echocardiogram. Measurements of time intervals were made with dial gauge callipers (Mitutoya Co, Japan) read to the nearest 0.1 mm (1.3 ms). Most measurements were made only once. When 34 measurements made independently by two observers were compared, 23 had differences <0.2 mm. The following five intervals were measured: RR, QT, S₁S₂, QS₁, and S₂T.

Maximum myocardial shortening rate was estimated by drawing a tangent to the fastest-moving component of the posterior wall echo (Fig. 1) and computing the cotangent of the angle between this line and the vertical reference. The slopes indicate only relative changes in rate, not absolute values. Consequently, shortening rate is expressed in terms of percentage changes with each intervention, relative to the control. The end-diastolic and end-systolic diameters were measured respectively as the dimensions at the peak of the R wave and the maximum anterior movement of the posterior wall.

Posterior wall motion was chosen to indicate

relative changes in maximum myocardial shortening mainly for simplicity. It required only a single measurement, that of an angle. Other indices, such as mean circumferential shortening, require several measurements, which increase the error of the estimate. Posterior wall motion has the added advantage that it reflects maximum rather than mean shortening velocity. It has the disadvantage that it results partly from circumferential fibre shortening and partly from overall movement of the left ventricle. Consequently, it does not indicate absolute myocardial shortening rate directly. It is assumed here, however, that ventricular movement was proportional to myocardial shortening in each individual in the same position. To the extent that this assumption is correct, the effects of ventricular movement cancel when calculating relative changes in velocity.

INTERVENTIONS

All recordings for each subject were made at a single time with the subject lying supine, his right side slightly raised, and with the echo transducer in the same position throughout. The order of the interventions was as follows. First a control recording was made with the subject lying quietly. Carotid massage was then applied several times to slow the pulse transiently. Next, the subject inhaled amyl nitrite, and recordings were made during the resulting tachycardia. Ten to 15 minutes later, when the tachycardia and flushing had subsided, 1.2 mg atropine was injected intravenously. Recordings were made during the peak of the ensuing tachycardia.

ANALYSIS

Measurements of 10 cardiac cycles were made for each intervention. The cycles chosen were those 10 that showed the greatest change in RR interval in response to the intervention, after excluding any record that could not be read because of respiratory interference. All measurements of the 10 cycles were averaged and the standard error of the mean computed. The size of the symbols along the Y axis in Fig. 2 and 3 (27 ms) was chosen so that of the 80 time intervals plotted, 68 had standard errors smaller than the symbols, and 18 had standard errors less than half the size of the symbols. Unless otherwise stated, significance of differences was calculated from the paired Student's *t* test taking the mean of 10 measurements for each individual as a single value. Those *p* values less than 0.05 were considered significant.

Results

The resting pulse rates ranged from 49 to 75 (mean 61). Carotid massage decreased the rates by an average of 15 per cent. Amyl nitrite increased the pulse rates by an average of 54 per cent, and atropine by 47 per cent, the difference being insignificant. The end-diastolic diameter was only slightly less with the amyl nitrite than with atropine (2.3%), but the end-systolic diameter was significantly decreased (12.5%, $p < 0.05$). The slope of the posterior wall motion was not significantly changed by carotid massage or atropine unless the heart rate increased to about 90/min, as has been found with mean circumferential fibre shortening using atrial pacing to vary heart rate.⁴ Posterior wall motion was increased significantly ($p < 0.01$) by amyl nitrite (Fig. 2A). The large difference in posterior wall motion, compared with approximately the same change in heart rate, allowed the effects of fibre shortening to be distinguished from those of heart rate.

The QT and S_1S_2 intervals both varied inversely with heart rate (Fig. 2B and C). Close inspection of the data in Fig. 2B and C shows, however, that for each individual, the QT interval was longer for the tachycardia produced by amyl nitrite than that produced by atropine, and that the reverse is true for the S_1S_2 interval.* The shorter S_1S_2 interval and the longer QT interval with amyl nitrite as

* Three different methods of analysis showed the differences to be significant: (1) the two-tailed, paired *t* test gave $p < 0.005$ for the QT and $p < 0.03$ for the S_1S_2 intervals; (2) the probability of obtaining the intervals for all five subjects deviating in the expected direction is $1/2^5 = 1/32$, yielding $p < 0.032$ for both the QT and S_1S_2 intervals; (3) when the unpaired *t* test was applied to the means for each individual, all five of the QT and three of the S_1S_2 interval differences yielded $p < 0.05$; two of the S_1S_2 and three of the QT interval differences yielded $p < 0.001$.

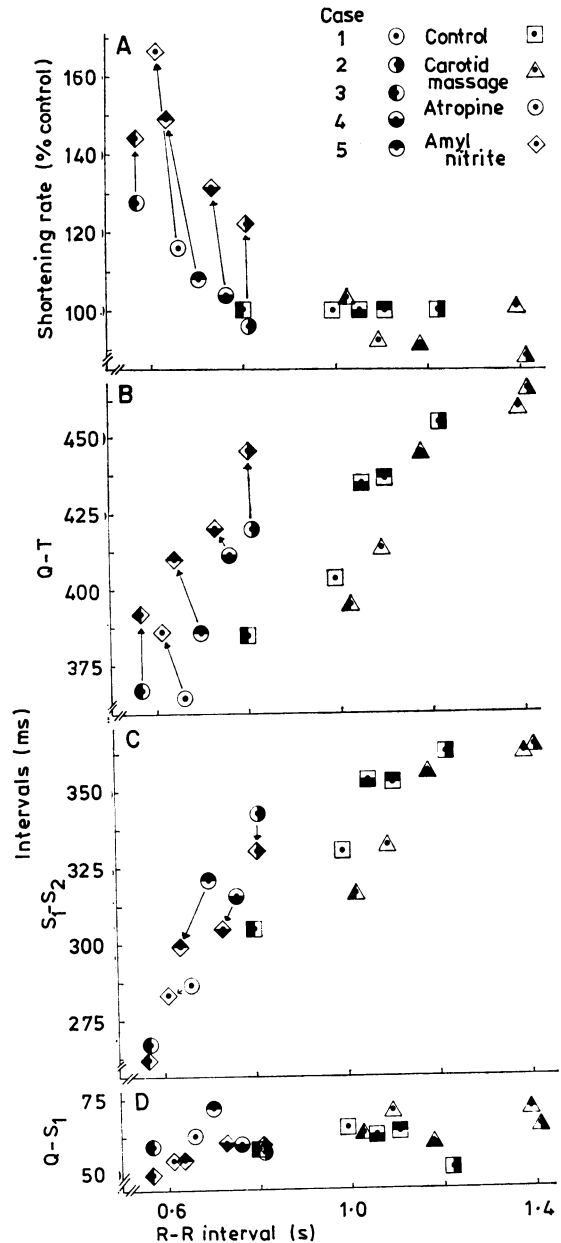


Fig. 2 Effect of RR interval and interventions on fibre shortening and time intervals: interventions are identified by shape and subjects by shading of symbols, according to key in inset. Shortening rates (A) are expressed as a percentage of the control values. Intervals (B, C, D) as described in text. The arrows in A, B, and C indicate the direction of changes with amyl nitrite, as compared with atropine, for each subject.

compared with atropine resulted in substantial increases in the S_2T intervals with amyl nitrite. This interval was found to correlate with changes in maximum fibre shortening, as indicated by changes in the slope of the posterior wall motion (Fig. 3A). Though the relation between fibre shortening and S_2T interval is probably not strictly linear, an estimate of the correlation between the two variables was obtained using a linear regression. For the data in Fig. 3A, the correlation coefficient was 0.67, and it was increased to 0.88 when the intervals were divided by the control values (Fig. 3B) to normalise the variation among the individuals. The S_2T interval did not correlate well with changes in heart rate.

The QS_1 interval was not significantly affected by any of the interventions (Fig. 2D), indicating that the changes in the S_2T intervals were largely the result of the changes in the QT and S_1S_2 intervals.

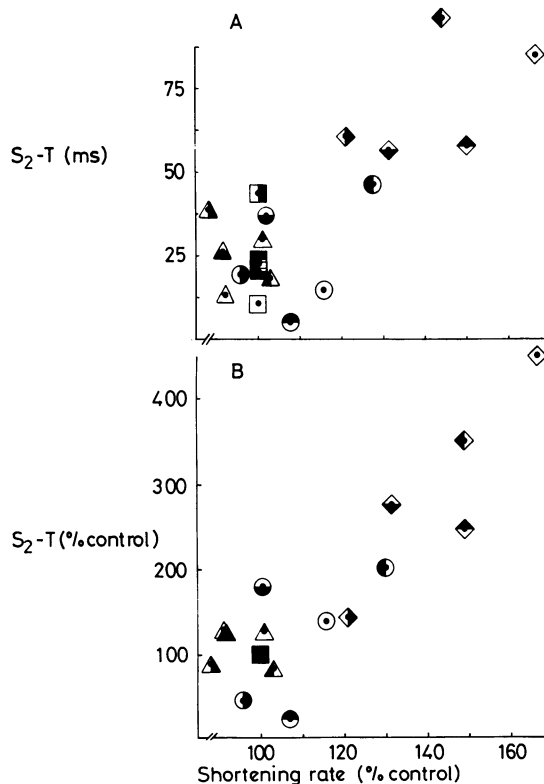


Fig. 3 Effect of maximum shortening rate on S_2T interval: same key for intervention and subjects as in Fig. 2. Intervals plotted in A have been normalised to subjects' control values in B.

Discussion

The findings that rapid myocardial shortening is associated with a longer QT interval and a shorter duration of mechanical systole are in keeping with studies in isolated muscle; but several other factors that might have contributed to these results should be considered. It is possible, for example, that the changes were the result of adrenergic stimulation during amyl nitrite. Catecholamines do shorten mechanical activation in isolated muscle,⁵ and might, therefore, be expected to decrease the S_1S_2 interval; however, these agents do not lengthen the duration of the ventricular action potential,⁶ making it unlikely that the increased S_2T interval after amyl nitrite was the result entirely of adrenergic influences. It should be mentioned that adrenergic stimulation has a variable influence on the QT interval in the intact animal.⁷ Indeed, it is possible that the variability derives from the secondary effects of muscle shortening. Direct inotropic stimulation of the ventricle, either by rapid catecholamine infusion or by left stellate ganglion stimulation, which would be expected to cause a more rapid myocardial shortening, prolongs the QT interval. By contrast, slower infusion of catecholamines or more extensive stimulation, which might raise peripheral vascular resistance sufficiently to prevent the increased myocardial shortening, produces no increase, and sometimes a decrease of the QT interval.⁷

It is also possible that the changes in the S_2T interval were the result of the smaller end-systolic ventricular volumes after amyl nitrite. It is difficult to distinguish changes caused by active muscle shortening from those caused by short lengths. For example, the duration of mechanical activity in isolated muscle can be reduced substantially at short lengths,⁸ but this effect is variable^{5,8} and the reduction is very much diminished when the series compliance in the preparation is made stiffer, minimising internal shortening during "isometric" contractions (Ford, unpublished observations). This result together with the finding that action potential duration is not influenced by muscle length⁹ suggest that the prolonged S_2T interval was not the result of a short end-systolic muscle length.

Although a prolonged QT or a shortened S_1S_2 interval have not previously been associated with rapid myocardial shortening, each has been described in coronary artery disease, where healthy myocardium might be expected to contract more rapidly, compensating for hypodynamic ventricular segments. For example, both changes have been described in acute myocardial infarction^{10,11} and persistence of these changes has been correlated

with a poor prognosis.^{12, 13} In addition, a prolonged QT interval has been correlated with a poor prognosis in chronic coronary artery disease¹³ and this might reflect, in part, the correlation of a poor prognosis with the degree of ventricular hypokinesia that has been found directly in angiographic studies.¹⁴

It would be expected from studies in isolated muscle,^{2, 3} and isolated hearts,¹⁵ that the relatively increased afterload imposed by cardiac failure would substantially increase the total duration of electromechanical systole (QS₂ interval). In fact, the reverse is usually found,^{16, 17} though there is substantial scatter in the results.¹⁷ The shortening of total systole might also be explained by inhomogeneities in ventricular contraction, with the rapidly contracting segments relaxing earlier. Varying degrees of hypokinesia in the patients with heart failure could explain the larger standard deviation of the QS₂ measurement in this population.

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